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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,398	11/19/2003	Fredericus Antonius Dijcks	O 97312 US C1	9720

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EXAMINER	
STOCKTON, LAURA LYNNE	
ART UNIT	PAPER NUMBER
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,398	DIJCKS ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

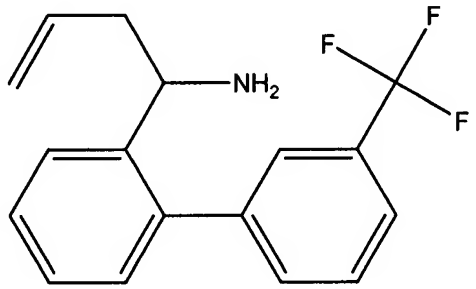
1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 23 and 25 are pending in the application.

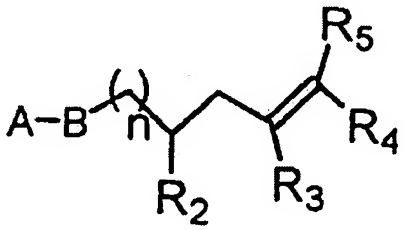
Election/Restrictions

Applicant's election with traverse of the species



2-(3-trifluoromethylphenyl)-alpha-2-propenyl-benzenemethanamine

compound (34) found on page 90 of the instant specification in the reply filed on April 28, 2006 and August 10, 2006 was acknowledged in the previous Office Action. The elected species is embraced by formula I (reproduced below), starting on page 58, last line,



(I)

wherein A is (a); Y is CH; X is CH=CH; P and S are each hydrogen; R_1 is on ring (a) is trifluoromethyl; B is (d); R^1 on ring (d) is hydrogen; R_2 is NH_2; n is zero; and R_3, R_4 and R_5 each represent hydrogen.

The requirement was deemed proper and therefore made FINAL in the previous Office Action.

As stated in the previous Office Action, the instant application has been examined according to M.P.E.P. 803.02. Since no prior art was found on the elected species for the instant claimed method of use, the search of the instant claimed invention was expanded until prior art was found and prior art applied. In Response to the previous Office Action, Applicant has amended the claims in the Amendment filed February 26, 2007 to overcome the cited prior art reference. The search was again expanded until prior

art was found and the search was then stopped and the prior art applied.

Claimed subject matter not embraced by the elected species nor the below applied prior art is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 28, 2006 and August 10, 2006.

The rejections of pending claims 23 and 25 under 35 USC § 102 and 35 USC § 103 over Morad et al. {U.S. Pat. 4,894,376} have been overcome by the amendment to claim 23.

Terminal Disclaimer

The terminal disclaimers filed on February 26, 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent 6,313,139 and U.S. Patent 6,080,773 have been reviewed and are accepted. The terminal disclaimers have been recorded.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using the compounds disclosed by the instant specification for treating anxiety by administering an I_h channel inhibitor having a pIC_{50} of

5 to 12 for inhibition of the hyperpolarization-activated cation current in dorsal root ganglion cells, does not reasonably provide enablement for making and treating anxiety by administering any compound presently known or will become known in the future which is an I_h channel inhibitor having a pIC_{50} of 5 to 12 for inhibition of the hyperpolarization-activated cation current in dorsal root ganglion cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

The nature of the invention

Applicant is claiming methods for treating anxiety by administering an effective amount of an I_h channel inhibitor which has a pIC_{50} of 5 to 12 for inhibition of the hyperpolarization-activated cation current in dorsal root ganglion cells. See, for example, instant claim 23. The instant claims do not recite a disclosed genus of any formula to represent an I_h channel inhibitor or any particular disclosed specie which represents an I_h channel inhibitor. From the reading of the specification, it appears that Applicant is asserting that any compound, because of its mode

action, which involves being a I_h channel modulator, would be useful for treating anxiety.

The amount of direction or guidance present and the presence or absence of working examples

That any compound that has an Ih channel inhibitor property can be used to treat anxiety is an incredible finding for which Applicant has not provided supporting evidence. Further, the instant specification fails to disclose or make all compounds that are considered I_h channel inhibitors.

The breadth of the claims

The breadth of the claims is treating anxiety by administering any compound that has been classified as an I_h channel inhibitor that has a pIC_{50} of 5 to 12 for inhibition of the hyperpolarization-activated cation current in dorsal root ganglion cells.

The quantity of experimentation needed

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine

which compounds exhibit the desired pharmacological activities for the disorder instantly claimed. The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to testing all presently known compounds, or compounds which may become known in the future and which are generically embraced in the claim language, and when faced with the unpredictability of the pharmaceutical art. Thus, factors such as "sufficient working examples", "the level of skill in the art" and predictability, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

The level of the skill in the art

Even though the level of skill in the pharmaceutical art is very high, based on the unpredictable nature of the invention and state of the prior art and lack of guidance and direction, one

skilled in the art could not use the claimed invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23 and 25 are indefinite because the metes and bounds of these claims cannot be ascertained since a compound that meets the definition of a Ih channel inhibitor is not recited in the instant claims.

Response to Arguments

Applicant's arguments filed February 26, 2007 have been fully considered but they are not persuasive.

Applicant has argued the rejection of the claims under 35 USC 112, first and second paragraphs. Applicant argues that the compounds identified as I_h channel have high selectivity when tested for their *in vitro* activity against a wide range of other receptor and ion channel targets and therefore, the skilled person would expect that the observed anti-anxiety activity of these compounds would be attributable to their I_h blocking properties and would be expected to have anti-anxiety activity. Applicant argues that the instant specification describes how to determine the potency and gives a specific test in mice for determining the compound's effect on anxiety and thus there is sufficient guidance in the specification. Applicant argues that the Office has not met the initial burden of providing objective evidence for lack of enablement.

All of Applicant's arguments have been considered but have not been found persuasive. Applicant is claiming a method for treating anxiety in an animal

comprising administering to said animal an effective amount of an I_h channel inhibitor, wherein said I_h channel inhibitor has a pIC_{50} of 5 to 12 for inhibition of the hyperpolarization-activated cation current in dorsal root ganglion cells. It is important to realize that claim 23 is drawn to a method of using a compound {i.e., an I_h channel inhibitor} but the claims provide no structural requirements of any kind. The compound could be small molecules or could be peptides or antibodies, etc. The compound could be organic or inorganic. How are these compounds, other than those disclosed in the instant specification, made? Where in the instant specification does it show how to make all of the compounds which meet the limitations of instant independent claim 23?

The compounds being administered for treating anxiety are instead defined in terms of properties. The fact that the tests for (1) determining whether the compound inhibits an I_h channel, (2) determining the

pIC_{50} values, and (3) determining the compounds effect on anxiety may be disclosed in the instant specification and may be considered routine does not necessarily preclude a finding of nonenablement given the scope of the claims. Note that in University of *Rochester v. G.D. Searle & Co.* 68 USPQ2d 1424 at 1438, the screening for over 600 compounds was deemed to be undue. Applicant's scope far exceeds this number. Additionally, and according to Applicant, each potential compound would have to undergo three different tests to determine if the limitations found in independent claim 23 have been met. The specification must teach how to make and use the invention, not teach how to figure out for oneself how to make and use the invention. *In re Gardner* , 166 USPQ 138 (CCPA 1970). Therefore, one skilled in the art could not make or use the claimed invention without undue experimentation. The claims are also indefinite

because the metes and bounds of the claims cannot be ascertained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gee et al. {U.S. Pat. 5,120,723}.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims a method for treating anxiety by administering an effective amount of an I_h inhibitor. Gee et al. teach a method of treating anxiety by

administering compounds which are modulators of the excitability of the central nervous system as mediated by their ability to regulate chloride ion channels associated with the GABA-benzodiazepine receptor complex (see entire document; specifically, column 3, lines 38-68; column 4, lines 55-67; and columns 5-7 and 10; and especially the compounds in Table 2 in columns 13-14).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference, if any, is the recitation of a particular pIC_{50} range as recited in the instant claimed claims.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814 (1964). The motivation to make the compounds of the

prior art derives from the expectation that structurally similar compounds would possess similar activity (e.g., treating anxiety). Since Gee et al. teach that the compounds treat anxiety, the compounds of Gee et al. must be an I_h channel inhibitor since a compound and its properties are inseparable. *In re Papesch*, 137 USPQ 43 (CCPA 1963).

One skilled in the art would thus be motivated to administer products embraced by the prior art to arrive at the instant claimed invention with the expectation of treating anxiety. The instant claimed invention would have been suggested and therefore, obvious to one skilled in the art.

The method of using the elected species of compound (34) found on page 90 of the instant specification for the purposes of the instant claimed invention is free of the prior art of record.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains subject matter drawn to an invention nonelected with traverse in the reply filed on April 28, 2006 and August 10, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the

automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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Patent Examiner
Art Unit 1626, Group 1620
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May 7, 2007